CTJ ORIGINAL

RMT

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF TEXAS
FORT WORTH DIVISION

GALDERMA LABORATORIES, L.P. and GALDERMA S.A., Plaintiffs,	§	
v.	§	**4-10 CV-114-A** **CAUSE NO.** _____
TARO PHARMACEUTICALS U.S.A., INC. and TARO PHARMACEUTICAL INDUSTRIES, LTD., Defendant.	§	**Jury Trial Requested**

ORIGINAL COMPLAINT

Plaintiffs, Galderma Laboratories, L.P. ("Galderma L.P.") and Galderma S.A. (collectively "Galderma"), as and for their Complaint against Defendants, Taro Pharmaceuticals U.S.A., Inc. and Taro Pharmaceutical Industries, Ltd., allege as follows:

THE PARTIES

1. Plaintiff Galderma Laboratories, L.P. is a Texas Limited Partnership, having a principal business address at 14501 North Freeway, Fort Worth, Texas 76177. As part of its business, Galderma Laboratories, L.P. is involved in the marketing and sale of pharmaceutical products.

2. Plaintiff Galderma S.A. is a Swiss corporation, with its principal business address at World Trade Center, Avenue de Gratta-Paille 2, Case Postale 453, CH-1000 Lausanne 30 Grey, Switzerland. As part of its business, Galderma S.A. is involved in the research, development, marketing, and sale of pharmaceutical products.

3. On information and belief, defendant Taro Pharmaceutical Industries Ltd. ("Taro") is an Israeli company, with its principal place of business at Euro Park, Italy Building,

Yakum Business Park, Yakum 60972, Israel. Taro Pharmaceutical Industries Ltd. may be served with process by and through its agent for service of process in the United States, Taro Pharmaceuticals U.S.A., Inc. 3 Skyline Drive, Hawthorne, NY, 10532.[1]

4. On information and belief, defendant Taro Pharmaceuticals U.S.A., Inc. ("Taro U.S.A." and, collectively with Taro, "Defendants") is a New York company, with its principal place of business at 3 Skyline Drive, Hawthorne, New York 10532. Taro U.S.A. may be served with process by and through its registered agent for service of process, CT Corporation System, 111 Eighth Avenue, New York, NY 10011.

JURISDICTION AND VENUE

5. This action arises under the patent laws of the United States of America, Title 35, United States Code. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

6. Defendants Taro and Taro U.S.A. are subject to personal jurisdiction in this District by virtue of, *inter alia*, their conduct of business in this District, their purposeful availment of the rights and benefits of Texas law, their substantial and continuing contacts with the State, and their knowledge that a Texas Limited Partnership located in this District would be injured by their actions. Upon information and belief, Defendants engage in the manufacture and sale of a range of generic pharmaceutical products within the United States generally and the State of Texas specifically.

7. Venue is proper in this district pursuant to 28 U.S.C. § 1391(c). For example, Plaintiff Galderma L.P. is located in this District, and Galderma's witnesses and documents will be material to this litigation. As another example, venue is appropriate in this District because

[1] *See* Taro Pharmaceutical Industries, Ltd. June 8, 2007 Letter to Shareholders at 19, *available at* http://www.taro.com/taronoticeandproxy.pdf.

the claims asserted herein arise out of an act of patent infringement (*i.e.*, Defendants' filing of the ANDA and issuance of the Paragraph IV Certification purposefully targeting a resident of this District (Galderma L.P.). As a further example, 21 U.S.C. § 355(j)(5)(C)(i)(II) establishes this District as the only proper venue in which Plaintiffs could file suit seeking a declaration of non-infringement in connection with the Abbreviated New Drug Application ("ANDA").

FACTS PERTINENT TO ALL CLAIMS FOR RELIEF

8. On August 22, 2000, the United States Patent and Trademark Office ("PTO") issued United States Patent No. 6,106,848 (the "'848 Patent") entitled "Topically Applicable O/W Emulsions Having High Glycol Content and At Least One Biologically Active Agent" to Centre International de Recherches Dermatologiques Galderma, the assignee of the named inventors Isabelle Preuilh and Nathalie Willcox. Centre International de Recherches Dermatologiques Galderma assigned the '848 Patent to Galderma S.A.. Galderma S.A. is the current assignee of the '848 Patent. A copy of the '848 Patent is attached hereto as Exhibit A.

9. The '848 Patent is valid, enforceable, and has not expired.

10. On July 24, 2003, the United States Food and Drug Administration ("FDA") approved New Drug Application ("NDA") No. 21-535 for clobetasol propionate lotion, 0.05%, which Galderma sells under the name Clobex.®

11. The '848 Patent is listed in the FDA publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (known as the "Orange Book") as covering Clobex® clobetasol propionate lotion, 0.05%.

12. On August 18, 2003, Galderma S.A. granted Galderma L.P. the exclusive right to distribute Clobex® Lotion in the United States.

13. On information and belief, Defendants engage in the manufacture and sale of a range of generic pharmaceutical products (including generic drug products manufactured and sold pursuant to an approved abbreviated new drug application) within the United States generally and the State of Texas specifically.

14. On information and belief, Defendants actively review pharmaceutical patents and seek opportunities to challenge those patents.

15. On information and belief, Defendants reviewed the '848 Patent and certain commercial and economic information relating to Clobex®, including estimates of the revenues generated by the sale of Clobex®, and decided to file an Abbreviated New Drug Application ("ANDA"), seeking approval to market clobetasol propionate lotion, 0.05%.

16. On information and belief, Defendants submitted to the FDA ANDA No. 200302 to seek approval to engage in the commercial manufacture, use, and sale of clobetasol propionate lotion, 0.05% prior to the expiration of the '848 Patent.

17. Plaintiffs received a letter dated January 8, 2010, from Defendants notifying Galderma that Defendants' ANDA No. 200302 includes a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (a "Paragraph IV certification") that, in Defendants' opinion, "the claims of the '848 Patent will not be infringed by the commercial manufacture, use or sale of the product that is the subject of Taro's ANDA."

18. Defendants were aware of the '848 Patent when they filed ANDA No. 200302 and a Paragraph IV certification.

19. Plaintiffs commenced this action within forty-five (45) days of the date that they received Defendants' Notice of ANDA No. 200302 containing the Paragraph IV certification.

20. On information and belief, Defendants intend to continue seeking approval of ANDA No. 200302 from the FDA and to engage in the commercial manufacture, marketing, and sale of clobetasol propionate lotion, 0.05% (including commercial marketing and sale of such a product in the State of Texas) in the event that FDA approves ANDA No. 200302.

FIRST CLAIM FOR RELIEF
(Infringement of the '848 Patent by Defendants)

21. Plaintiffs repeat and reallege each and every allegation contained in paragraphs 1 through 20 hereof, as if fully set forth herein.

22. Through the conduct alleged above, Defendants have infringed, and continue to infringe, one or more claims of the '848 Patent.

23. By filing ANDA No. 200302 with a Paragraph IV certification seeking FDA approval to engage in the commercial manufacture, use, and sale of clobetasol propionate lotion, 0.05%, prior to the expiration of the '848 Patent, Defendants have infringed the '848 Patent under 35 U.S.C. § 271(e)(2).

24. Defendants were aware of the existence of the '848 Patent prior to filing ANDA No. 200302.

25. Plaintiffs will be irreparably harmed if Defendants are not enjoined from infringing the '848 Patent.

CONTINGENT JURY DEMAND

If Defendants should launch a product during the pendency of this litigation, and Plaintiffs incur damages, then Plaintiffs will demand damages and trial by jury of all issues and claims alleged herein.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs hereby request the following relief:

(A) An order adjudging and decreeing that Defendants have infringed the '848 Patent;

(B) An order pursuant to 35 U.S.C. § 271(e)(4)(A) decreeing that the effective date of any approval of ANDA No. 200302 be no earlier than the expiration date of the '848 Patent, including any extensions;

(C) A preliminary and permanent injunction pursuant to 35 U.S.C. §§ 271(e)(4)(B) restraining and enjoining Defendants and their officers, agents, servants, employees, and those acting in privity or concert with any of them from engaging in the commercial manufacture, use, offer for sale, or sale within the United States, or importation into the United States, of the clobetasol propionate products described in ANDA No. 200302 or any other ANDA not colorably different from ANDA No. 200302 until the expiration date of the '848 Patent, including any extensions;

(D) An award to Plaintiffs, pursuant to 35 U.S.C. § 271(e)(4)(C), of damages and other monetary relief, as a result of Defendants' infringement, to the extent there has been any commercial manufacture, use, offer to sell, or sale within the United States or importation into the United States of the clobetasol propionate lotion, 0.05%, described in ANDA No. 200302 prior to expiration of the '848 Patent; and

(E) Such other and further relief as this Court may deem just and proper.

Respectfully submitted,

Michael C. Wilson
Texas State Bar No. 21704590
Jamil N. Alibhai
Texas State Bar No. 00793248
Daniel E. Venglarik
Texas State Bar No. 00791851
MUNCK CARTER, LLP
600 Banner Place
12770 Coit Road
Dallas, Texas 75251
Telephone: (972) 628-3600
Facsimile: (972) 628-3616

ATTORNEYS FOR PLAINTIFFS

EXHIBIT A

U 1663012

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

October 12, 2007

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THIS OFFICE OF:

U.S. PATENT: *6,106,848*

ISSUE DATE: *August 22, 2000*

By Authority of the

Under Secretary of Commerce for Intellectual Property

and Director of the United States Patent and Trademark Office

P. R. Grant

P. R. GRANT

Certifying Officer

US006106848A

United States Patent [19]

Preuilh et al.

[11] Patent Number: 6,106,848

[45] Date of Patent: *Aug. 22, 2000

[54] **TOPICALLY APPLICABLE O/W EMULSIONS HAVING HIGH GLYCOL CONTENT AND AT LEAST ONE BIOLOGICALLY ACTIVE AGENT**

[75] Inventors: **Isabelle Preuilh**, Le Canet; **Nathalie Willcox**, Le Rouret, both of France

[73] Assignee: **Centre International de Recherches Dermatologiques**, Valbonne, France

[*] Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

[21] Appl. No.: **08/935,054**

[22] Filed: **Sep. 22, 1997**

[30] **Foreign Application Priority Data**

Sep. 20, 1996 [FR] France 96 11510

[51] **Int. Cl.**[7] **A61K 9/07**; A61K 47/10; A61K 47/14; A61K 47/30

[52] **U.S. Cl.** **424/401**; 424/59; 424/62; 424/63; 424/65; 424/70.1; 424/70.6; 424/70.8; 424/70.9; 424/70.11; 424/70.16; 424/70.21; 424/70.22; 424/73; 523/105; 523/122; 514/818; 514/852; 514/859; 514/864; 514/875; 514/880; 514/882; 514/886; 514/887; 514/937; 514/938; 514/939; 514/940; 514/941

[58] **Field of Search** 523/102–105, 523/122; 524/386; 510/158–160; 574/817, 818, 825, 828, 844–848, 852, 855, 865, 871, 873–875, 880–882, 886, 887, 928, 937–941, 947; 424/405, 401, 59

[56] **References Cited**

FOREIGN PATENT DOCUMENTS

0268164	5/1988	European Pat. Off. .
0279641	8/1988	European Pat. Off. .
0347225	12/1989	European Pat. Off. .
2646435	4/1978	Germany .
94/17830	8/1994	WIPO .

Primary Examiner—Neil S. Levy
Attorney, Agent, or Firm—Burns, Doane, Swecker & Mathis, L.L.P.

[57] **ABSTRACT**

Stable, topically applicable oil-in-water bioaffecting emulsions having intermediate viscosity, characteristically ranging from 3 to 10 Pa·s, comprise (a) from 30% to 50% by weight of at least one pro-penetrating glycol, (b) at least one emulsifying agent, advantageously an anionic amphiphilic polymer, and (c) at least one biologically active agent, for example an active agent that modulates skin differentiation and/or proliferation and/or pigmentation, an anti-inflammatory, an antibacterial, an antifungal, etc.

20 Claims, No Drawings

TOPICALLY APPLICABLE O/W EMULSIONS HAVING HIGH GLYCOL CONTENT AND AT LEAST ONE BIOLOGICALLY ACTIVE AGENT

This application claims benefit of priority under 35 U.S.C. §119 to French Application No. 96-11510, filed on Sep. 20, 1996.

BACKGROUND OF THE INVENTION

1. Technical Field of the Invention

The present invention relates to novel topically applicable oil-in-water (O/W) emulsions comprising a high content of at least one pro-penetrating glycol, an appropriate emulsifying system and at least one biologically active agent.

2. Description of the Prior Art

Currently marketed are numerous topical compositions comprising an active agent and a high content of glycol, the latter promoting the penetration of the biologically active agent into the skin. Given the high content of pro-penetrating glycol, these compositions are formulated as emulsions having a high content of fatty phase which are also commonly designated "lipocreams," as anhydrous compositions which are deemed "ointments," as fluid compositions having a high content of volatile solvents, such as ethanol or isopropanol, which are destined for application to the scalp, i.e., "hair lotions," or, alternatively, as viscous O/W emulsions which are also designated "O/W creams."

O/W creams comprising a corticoid and including a high percentage of propylene glycol (47.5%), which are marketed under the trademark TEMOVATE® by GLAXO, are known to this art. Indeed, the stabilization of a formulation comprising such a percentage of glycol necessitates incorporating, in the emulsion, emulsifying and stabilizing agents of the glyceryl stearate or PEG 100 stearate type or, alternatively, stabilizing agents or consistency factors of the white wax or ketostearyl alcohol type which form a viscous cream, namely, whose viscosity is greater than 10 Pa·s (10,000 centipoises, measured with a Brookfield apparatus model LVDV II+paddle No. 4, at a speed of 30 revolutions/min for 30 seconds and at a temperature of 25° C.±3° C.).

To facilitate the application of topical compositions comprising a high percentage of glycol, it would be desirable to provide novel formulations of the O/W emulsion type, whose viscosity would be intermediate between the hair lotions which are too fluid and the use of which is too limited, and the O/W creams which are too viscous and which have a fatty and sticky characteristic, while preserving the propenetrating properties of the glycol.

SUMMARY OF THE INVENTION

Accordingly, a major object of the present invention is the provision of novel topically applicable oil-in-water (O/W) emulsions, comprising from 30% to 50% by weight relative to the total weight of the composition of at least one glycol, an appropriate emulsifying system and at least one biologically active agent.

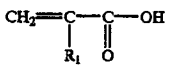
DETAILED DESCRIPTION OF BEST MODE AND SPECIFIC/PREFERRED EMBODIMENTS OF THE INVENTION

More particularly according to the present invention, by "fluid emulsion" is advantageously intended an emulsion whose viscosity ranges from 3 to 10 Pa·s (3,000 to 10,000 centipoises), a viscosity measured with a Brookfield apparatus model LVDV II+paddle No. 4, at a speed of 30 revolutions/min for 30 seconds and at a temperature of 25° C.±3° C.

Advantageously, a stable emulsion is provided according to the invention by selecting, as an appropriate emulsifying system, at least one polymeric emulsifier. The polymeric emulsifiers are in particular described by CLYMANS & BRAND in "Cosmetics and Toiletries" (manufacture worldwide, 1995, 119–125).

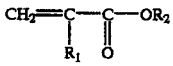
These are, in particular, anionic amphiphilic polymers, more especially those comprising at least one hydrophilic recurring structural unit of the unsaturated olefin carboxylic acid type, and at least one hydrophobic recurring structural unit of the C_{10}–C_{30} alkyl ester type.

According to the invention, acrylic structural units are those of the formula:



in which R_1 is H, CH_3 or C_2H_5, namely, acrylic acid, methacrylic acid or ethacrylic acid structural units.

Alkyl acrylate structural units are those of the formula:



in which R_1 is H, CH_3 or C_2H_5, namely, acrylate, methacrylate or ethacrylate units, and R_2 is a C_{10}–C_{30}, preferably C_{12}–C_{22}, alkyl radical.

Exemplary acrylates according to the invention include lauryl acrylate, stearyl acrylate, decyl acrylate, isodecyl acrylate, dodecyl acrylate and the corresponding methacrylates, lauryl methacrylate, stearyl methacrylate, decyl methacrylate, isodecyl methacrylate and dodecyl methacrylate.

Preferably, the above anionic amphiphilic polymers are crosslinked using a crosslinking polymerizable comonomer containing a CH_2=C< group with at least one other polymerizable group whose sites of unsaturation are not conjugated relative to each other.

Exemplary such crosslinking polymerizable comonomers preferably include polyallyl ethers such as, in particular, polyallylsucrose and polyallylpentaerythritol.

Crosslinked polymers of this type are well known to this art; they are, in particular, described in U.S. Pat. Nos. 3,915,921 and 4,509,949.

According to the invention, anionic amphiphilic polymers are preferred which comprise 95% to 60% by weight of acrylic recurring structural units, 4% to 40% by weight of acrylate recurring structural units and 0.1% to 6% by weight of crosslinking monomer, or (ii) which comprise 98% to 96% by weight of acrylic recurring structural units, 1% to 4% by weight of acrylate recurring structural units and 0.1% to 0.6% by weight of crosslinking monomer.

Among said crosslinked polymers indicated above, those marketed by GOODRICH under the trademarks PEMULEN TR1, PEMULEN TR2, CARBOPOL 1342 and CARBOPOL 1382 are most particularly preferred according to the present invention.

The compositions according to the invention advantageously comprise up to 1 by weight of appropriate emulsifying system, preferably from 0.2% to 0.4% by weight relative to the total weight of the composition.

The pro-penetrating glycol is advantageously selected from among propylene glycol, dipropylene glycol, propylene glycol dipelargonate, lauroglycol or ethoxydiglycol.

Preferably, the compositions according to the invention comprise from 40% to 50% by weight of pro-penetrating glycol.

Exemplary active agents according to this invention include the agents modulating skin differentiation and/or proliferation and/or pigmentation such as retinoic acid and isomers thereof, retinol and esters thereof, retinal, retinoids, in particular those described in FR-2,570,377, EP-199,636, EP-325,540, EP-402,072, vitamin D and derivatives thereof, estrogens such as estradiol, kojic acid or hydroquinone; antibacterial agents such as clindamycin phosphate, erythromycin or the tetracycline class of antibiotics; antiparasitic agents, in particular metronidazol, crotamiton or pyrethrinoids; antifungal agents, in particular compounds belonging to the class of imidazoles such as econazole, ketoconazole or miconazole or salts thereof, polyene compounds such as amphotericin B, compounds of the family of allylamines, such as terbinafine or alternatively octopirox; steroidal anti-inflammatory agents such as hydrocortisone, anthralins (dioxyanthranol), anthranoids, betamethasone valerate or clobetasol propionate, or non-steroidal anti-inflammatory agents such as ibuprofen and salts thereof, diclofenac and salts thereof, acetylsalicylic acid, acetaminophen or glycyrrhetinic acid; anaesthetic agents such as lidocaine hydrochloride and derivatives thereof; antipruritic agents such as thenaldine, trimeprazine or cyproheptadine; antiviral agents such as acyclovir; keratolytic agents such as alpha- and beta-hydroxycarboxylic or beta-ketocarboxylic acids, their salts, amides or esters and more particularly the hydroxy acids such as glycolic acid, lactic acid, malic acid, salicylic acid, citric acid and, in general, the fruit acids, and 5-n-octanoylsalicylic acid; anti-free radical agents such as alpha-tocopherol or esters thereof, superoxide dismutases, certain metal chelators or ascorbic acid and esters thereof; antiseborrhoeic agents such as progesterone; antidandruff agents such as octopirox or zinc pyrithione; anti-acne agents such as retinoic acid, benzoyl peroxide or adapalene; antimetabolites; agents for combating hair loss such as minoxidil; antiseptics.

Advantageously, the compositions according to the invention comprise from 0.0001% to 20% by weight relative to the total weight of the composition of at least one active agent, preferably from 0.025% to 15% by weight.

Of course, the amount of active agent in the compositions according to the invention will depend on the active agent under consideration. Thus, for a steroidal anti-inflammatory agent, the compositions according to the invention will advantageously comprise less than 1% by weight of active agent, preferably from 0.025% to 0.05% by weight. For the hydroquinones, the compositions according to the invention will preferably comprise from 2% to 5% of active agent. For the antibacterial or antifungal agents such as econazole, the compositions of this invention will preferably comprise from 8% to 10% by weight of active agent.

The fatty phase of the emulsion according to the invention may comprise fatty substances normally used in the intended field of application.

Among these, representative are the silicone fatty substances such as the silicone oils, as well as the non-silicone fatty substances such as the vegetable, mineral, animal or synthetic oils.

Exemplary silicone fatty substances include:

(i) the poly(C_1–C_{20} alkyl)siloxanes and, in particular, those having trimethylsilyl terminal groups, preferably those whose viscosity is less than 0.06 m^2/s, among which are included the linear polydimethylsiloxanes and the alkylmethylpolysiloxanes such as cetyldimethicone (CTFA name),

(ii) the volatile silicone oils, such as:

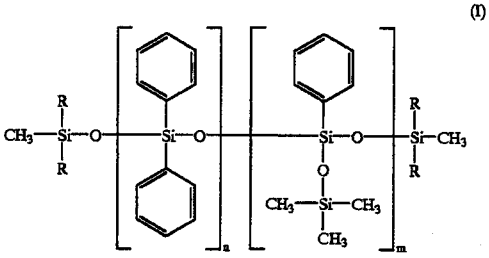
(a) the cyclic volatile silicones having from 3 to 8 silicon atoms and preferably from 4 to 5; these include, for example, cyclotetradimethylsiloxane, cyclopentadimethylsiloxane or cyclohexadimethylsiloxane,

(b) the cyclocopolymers of the dimethylsiloxane/methylalkylsiloxane type, such as SILICONE FZ 3109 marketed by UNION CARBIDE, which is a dimethylsiloxane/methyloctylsiloxane cyclocopolymer,

(c) the linear volatile silicones having from 2 to 9 silicon atoms; these include, for example, hexamethyldisiloxane, hexyl heptamethyltrisiloxane or octyl heptamethyltrisiloxane,

(iii) the phenylated silicone oils, in particular those having the structural formula (I):

(I)



in which R is a C_1–C_{30} alkyl radical, an aryl radical or an aralkyl radical; n is an integer ranging from 0 to 100, and m is an integer ranging from 0 to 100, with the proviso that the sum n+m ranges from 1 to 100.

Among the nonsilicone fatty substances, exemplary are the conventional oils such as paraffin oil, petroleum jelly, almond oil, perhydrosqualene, apricot oil, wheat germ, sweet almond, calophyllum, palm, castor, avocado, jojoba, olive or cereal germ oil; esters of fatty acids or of fatty alcohols, such as octyl dodecyl myristate or C_{12}–C_{15} alkyl benzoates, alcohols; acetylglycerides; octanoates, decanoates or ricinoleates of alcohols or of polyalcohols; triglycerides of fatty acids; glycerides; hydrogenated polyisobutene, hydrogenated oils which are solid at 25° C.; lanolins; fatty esters which are solid at 25° C.

These fatty substances may, in particular, be variously selected by one skilled in this art such as to provide a composition having the desired properties, for example as regards consistency or texture.

Thus, the fatty phase of the emulsion according to the invention may constitute from 5% to 50% by weight relative to the total weight of the composition, and preferably from 15% to 25% by weight.

The aqueous phase of the emulsions according to the invention may comprise water, a floral water such as cornflower water, or a natural mineral or thermal water, for example selected from among Vittel water, water from the Vichy basin, Uriage water, Roche Posay water, Bourboule water, Enghien-les-Bains water, Saint Gervais-les-Bains water, Nèris-les-Bains water, Allevard-les-Bains water, Digne water, Maizières water, Neyrac-les-Bains water, Lons-le-Saunier water, Bonnes water, Rochefort water, Saint

Christau water, Fumades water, Tercis-les-bains water, Avène water or Aix les Bains water.

The aqueous phase advantageously comprises from 10% to 70% by weight relative to the total weight of the composition, preferably from 20% to 40% by weight.

The pH of the compositions according to the invention advantageously ranges from 5 to 7, preferably from 5.5 to 6.5. It will be adjusted to the desired value by adding customary inorganic or organic bases or acids.

Moreover, the compositions according to the invention may comprise from 0% to 3% by weight, preferably from 0% to 2% by weight, relative to the total weight of the composition, of at least one coemulsifier which is advantageously selected from among esters of saturated or unsaturated fatty acids, which are natural or synthetic, in particular oleic acid or (iso)stearic acid, such as the esters of polyglycerin and isostearic acid which are marketed under the trademark LAMEFORM TGI by SIDOBRE-SINNOVA HENKEL, sorbitan isostearate marketed under the trade mark ARLACEL 987 by ICI, sorbitan sesquioleate marketed under the trademark ARLACEL 83 by ICI, the esters of glycol and isostearic acid such as PEG-6 isostearate marketed under the trademark OLEPAL ISOSTEARIQUE by GATTEFOSSE, the esters of sorbitol and oleic acid such as the polysorbates marketed under the trademark TWEEN by ICI, the fatty alcohol ethers, in particular oleyl alcohol, in particular the esters of glycol and oleyl alcohol, such as the oleths marketed under the trademark BRIJ by ICI, oxyethylenated sorbitan monostearate, the fatty alcohols such as stearyl alcohol or cetyl alcohol.

In addition, the compositions according to the invention may comprise at least one gelling and/or thickening agent in preferred concentrations ranging from 0% to 5% by weight relative to the total weight of the composition.

The gelling and/or thickening agent is advantageously selected from among:

(a) the polysaccharide biopolymers such as xanthan gum, carob gum, guar gum, alginates, modified celluloses such as hydroxyethylcellulose, methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carboxymethylcellulose,

(b) the synthetic polymers such as the polyacrylic acids, for example, glyceryl poly(meth)acrylate polymers such as HISPAGEL or LUBRAGEL marketed by HISPANO QUIMICA or GARDIAN, polyvinylpyrrolidone, polyvinyl alcohol, the crosslinked polymers of acrylamide and ammonium acrylate such as PAS 5161 or BOZEPOL C marketed by HOECHST, the crosslinked polymers of acrylamide and partially or completely neutralized 2-acrylamido-2-methylpropanesulfonic acid such as SEPIGEL 305 marleted by SEPPIC, the crosslinked polymers of acrylamide and methacryloyloxyethyltrimethylammonium chloride such as SALCARE SC 92 marketed by ALLIED COLLOIDS, the crosslinked polymers of acrylic acid and alkyl ethers of sucrose or of pentaerythritol (carbomers) such as CARBOPOL 910 to 934 marketed by GOODRICH.

The subject emulsions may comprise, in addition, any additive or adjuvant customarily employed in the cosmetic or pharmaceutical field, such as antioxidants, colorants, perfumes, essential oils, preservatives, cosmetic active agents, moisturizers, vitamins, essential fatty acids, sphingolipids, selftanning compounds such as DHA, sunscreening agents, fat-soluble polymers, in particular those which contain hydrocarbons, such as polybutene, polyalkylenes, polyacrylates and silicone polymers which are compatible with fatty substances. Of course, one skilled in this art will take care to select this or these possible additional compound(s), and/or their quantity, such that the advantageous properties of the compositions according to the invention are not, or not substantially, altered by the intended addition.

These additives and adjuvants may be present in the subject compositions in an amount of 0% to 10% by weight relative to the total weight of the composition.

In order to further illustrate the present invention and the advantages thereof, the following specific examples are given, it being understood that same are intended only as illustrative and in nowise limitative.

In said examples to follow, all parts and percentages are given by weight.

EXAMPLE 1

Example of a Specific Formulation According to the Invention

COMPOSITION:	% by weight
Purified water	qs 100
Hydroxypropylmethylcellulose	0.10
Propylene glycol	47.50
Active agent	0.05
Liquid paraffin 110–230	20.00
Acrylate/C_{10}–C_{30} alkyl acrylate crosslinked polymer (marketed under the trademark PEMULEN TR-2 by GOODRICH)	0.30
PEG-6 isostearate	2.00
NaOH, 10%	qs pH 6

In this formulation, the active agent remained stable for at least 3 months at 40° C.

EXAMPLE 2

Activity of Formulation Comprising Clobetasol Propionate

The formulation of Example 1 according to the invention comprised clobetasol propionate as the active agent.

Vasoconstriction tests according to the modified Stoughton protocol were performed in comparison with the corresponding O/W cream marketed under the trademark TEMOVATE by GLAXO.

The results evidenced an identical bioactivity for the two formulae, which confirmed that, despite the modification of the viscosity of the formulation according to the invention and the use of a different emulsifying system, the pro-penetrating glycol retained its pro-penetrating properties.

While the invention has been described in terms of various preferred embodiments, the skilled artisan will appreciate that various modifications, substitutions, omissions, and changes may be made without departing from the spirit thereof. Accordingly, it is intended that the scope of the present invention be limited solely by the scope of the following claims, including equivalents thereof.

What is claimed is:

1. A stable, topically applicable oil-in-water emulsion which is topically applicable to skin having intermediate viscosity, comprising (a) from 30% to 50% by weight relative to the total weight of said emulsion of at least one glycol, (b) at least one emulsifying agent comprising an

anionic amphiphilic polymer, and (c) at least one biologically active agent, wherein said anionic amphiphilic polymer is present in an amount which in the absence of another emulsifying agent results in an emulsion having an intermediate viscosity, wherein said intermediate viscosity is a viscosity which ranges from 3 to 10 Pa·s (3,000 to 10,000 centipoises), measured with a Brookfield viscometer LVDV II+paddle No. 4, at a speed of 30 revolutions/minutes for thirty seconds, and at a temperature of 25° C.±3° C.

2. The oil-in-water emulsion as defined by claim **1**, comprising up to 5% by weight relative to the total weight of said emulsion of at least one gelling and/or thickening agent.

3. The oil-in-water emulsion as defined by claim **1**, having a pH ranging from 5 to 7.

4. The oil-in-water emulsion as defined by claim **3**, having a pH ranging from 5.5 to 6.5.

5. The oil-in-water emulsion as defined by claim **1**, wherein said at least one polymeric emulsifier is a crosslinked anionic amphiphilic polymer.

6. The oil-in-water emulsion as defined by claim **1**, said anionic amphiphilic polymer comprising the copolymerizate of olefinically unsaturated carboxylic and C_{10}–C_{30} alkyl ester comonomers.

7. The oil-in-water emulsion as defined by claim **5**, said anionic amphiphilic polymer being crosslinked with olefinically unsaturated and non-conjugated polyolefinically unsaturated comonomers.

8. The oil-in-water emulsion as defined by claim **7**, said non-conjugated polyolefinically unsaturated comonomer comprising a polyallyl ether.

9. The oil-in-water emulsion as defined by claim **5**, said crosslinked anionic amphiphilic polymer comprising from 95% to 60% by weight of recurring acrylic structural units, from 4% to 40% by weight of recurring acrylate structural units, and 0.1% to 6% by weight of a crosslinking comonomer, wherein said percentages are relative to the total weight of said emulsion.

10. The oil-in-water emulsion as defined by claim **5**, said crosslinked anionic amphiphilic polymer comprising from 98% to 96% by weight of recurring acrylic structural units, from 1% to 4% by weight of recurring acrylate structural units, and 0.1% to 0.6% by weight of a crosslinking comonomer, wherein said weight percentages are relative to the total weight of said emulsion.

11. The oil-in-water emulsion as defined by claim **1**, comprising up to 1% by weight of said at least one emulsifying agent (b).

12. The oil-in-water emulsion as defined by claim **11**, comprising from 0.2% to 0.4% by weight of said at least one emulsifying agent (b).

13. The oil-in-water emulsion as defined by claim **1**, said at least one glycol (a) comprising a glycol, which promotes penetration of said emulsion into the skin selected from a glycol selected from the group consisting of propylene glycol, dipropylene glycol, propylene glycol dipelargonate, lauroglycol and ethoxydiglycol.

14. The oil-in-water emulsion as defined by claim **13**, comprising from 40% to 50% by weight relative to the total weight of said emulsion of said at least one glycol (a).

15. The oil-in-water emulsion as defined by claim **2**, said at least one biologically active agent is selected from the group consisting of (c) an agent which modulates at least one of skin differentiation, proliferation and pigmentation; an antibacterial agent, an antiparasitic agent, an antifungal agent, a steroidal anti-inflammatory agent, a non-steroidal anti-inflammatory agent, an anaesthetic agent, an antipruritic agent, an antiviral agent, a keratolytic agent, an anti-free radical agent, an antiseborrhoeic agent, an antidandruff agent, an anti-acne agent, an antimetabolite, an agent for combating hair loss, an antiseptic and combinations thereof.

16. The oil-in-water emulsion as defined by claim **15**, comprising from 0.0001% to 20% by weight relative to the total weight of said emulsion of said at least one biologically active agent (c).

17. The oil-in-water emulsion as defined by claim **1**, comprising from 5% to 50% by weight relative to the total weight of said emulsion of an oily phase.

18. The oil-in-water emulsion as defined by claim **17**, comprising from 10% to 70% by weight of an aqueous phase relative to the total weight of said emulsion.

19. The composition of claim **1**, wherein said anionic amphiphilic polymer comprises recurring acrylic structural units and acrylate structural units.

20. The composition of claim **2**, wherein said anionic amphiphilic polymer is cross-linked.

* * * * *

ORIGINAL

JS 44 (TXND Rev. 12/10)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

I. (a) PLAINTIFFS

Galderma Laboratories, L.P. and Galderma S.A.

(b) County of Residence of First Listed Plaintiff Tarrant County, TX
(EXCEPT IN U.S. PLAINTIFF CASES)

(c) Attorney's (Firm Name, Address, and Telephone Number)
Munck Carter, LLP
12770 Coit Road, Suite 600, Dallas, Texas 75251
(972)628-3600

DEFENDANTS

Taro Pharmaceuticals, U.S.A., Inc. and Taro Pharmaceutical Industries, Ltd.

County of Residence of First Listed Defendant Weschester County, NY
(IN U.S. PLAINTIFF CASES ONLY)

NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE LAND INVOLVED.

Attorneys (If Known)

4-10 CV-114-A

II. BASIS OF JURISDICTION (Place an "X" in One Box Only)

- ☐ 1 U.S. Government Plaintiff
- ☒ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

III. CITIZENSHIP OF PRINCIPAL PARTIES (Place an "X" in One Box for Plaintiff and One Box for Defendant)
(For Diversity Cases Only)

	PTF	DEF		PTF	DEF
Citizen of This State	☐ 1	☐ 1	Incorporated *or* Principal Place of Business In This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated *and* Principal Place of Business In Another State	☐ 5	☐ 5
Citizen or Subject of a Foreign Country	☐ 3	☐ 3	Foreign Nation	☐ 6	☐ 6

IV. NATURE OF SUIT (Place an "X" in One Box Only)

CONTRACT
- ☐ 110 Insurance
- ☐ 120 Marine
- ☐ 130 Miller Act
- ☐ 140 Negotiable Instrument
- ☐ 150 Recovery of Overpayment & Enforcement of Judgment
- ☐ 151 Medicare Act
- ☐ 152 Recovery of Defaulted Student Loans (Excl. Veterans)
- ☐ 153 Recovery of Overpayment of Veteran's Benefits
- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

TORTS

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury

PERSONAL INJURY
- ☐ 362 Personal Injury - Med. Malpractice
- ☐ 365 Personal Injury - Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

CIVIL RIGHTS
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 444 Welfare
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities - Other
- ☐ 440 Other Civil Rights

PRISONER PETITIONS
- ☐ 510 Motions to Vacate Sentence

Habeas Corpus:
- ☐ 530 General
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

FORFEITURE/PENALTY
- ☐ 610 Agriculture
- ☐ 620 Other Food & Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
- ☐ 640 R.R. & Truck
- ☐ 650 Airline Regs.
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Mgmt. Relations
- ☐ 730 Labor/Mgmt.Reporting & Disclosure Act
- ☐ 740 Railway Labor Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Empl. Ret. Inc. Security Act

IMMIGRATION
- ☐ 462 Naturalization Application
- ☐ 463 Habeas Corpus - Alien Detainee
- ☐ 465 Other Immigration Actions

BANKRUPTCY
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☒ 830 Patent
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DJWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

OTHER STATUTES
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Sat TV
- ☐ 810 Selective Service
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 890 Other Statutory Actions
- ☐ 891 Agricultural Acts
- ☐ 892 Economic Stabilization Act
- ☐ 893 Environmental Matters
- ☐ 894 Energy Allocation Act
- ☐ 895 Freedom of Information Act
- ☐ 900Appeal of Fee Determination Under Equal Access to Justice
- ☐ 950 Constitutionality of State Statutes

V. ORIGIN (Place an "X" in One Box Only)

☒ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from another district (specify) ☐ 6 Multidistrict Litigation ☐ 7 Appeal to District Judge from Magistrate Judgment

VI. CAUSE OF ACTION

Cite the U.S. Civil Statute under which you are filing **(Do not cite jurisdictional statutes unless diversity)**:

Brief description of cause:
Patent infringement action.

VII. REQUESTED IN COMPLAINT:

☐ CHECK IF THIS IS A **CLASS ACTION** UNDER F.R.C.P. 23

DEMAND $

CHECK YES only if demanded in complaint:
JURY DEMAND: ☑ Yes ☐ No

VIII. RELATED CASE(S) PENDING OR CLOSED: (See instructions)

JUDGE Terry R. Means DOCKET NUMBER 4:06-CV-0471-Y

DATE 02/19/2010

SIGNATURE OF ATTORNEY OF RECORD Michael C. Wilson w/p YAL

FOR OFFICE USE ONLY

RECEIPT # FW12234 AMOUNT 350 APPLYING IFP JUDGE A MAG. JUDGE

UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF TEXAS

Civil Filing Notice - Fort Worth Division

CIVIL ACTION NO: 4-10 CV-114-A

This case has been assigned to District Judge: _____

(Complete if applicable)
TRANSFERRED FROM: _____ DATE FILED: _____

Civil cases are assigned to a judge by random draw. A docket clerk for each judge maintains the recording of documents filed with the Clerk. A complete list of phone numbers for both the judges' chambers and the docket clerks is provided.

Judge	Court Settings	Pleadings Filed
(A) Judge John H. McBRYDE	(817)850-6650	(817)850-6611
Even Cases: 850-6652 Odd Cases: 850-6653		
(Y) Judge Terry R. MEANS	(817)850-6673	(817)850-6612
(BE) Magistrate Judge Charles BLEIL	(817)850-6690	(817)850-6697

For access to local rules, attorney admission information, frequently asked questions, common forms, filing instructions, and records information, please visit our web site at **www.txnd.uscourts.gov**. To speak to someone in the district clerk's office, please call (817) 850-6601.

To receive electronic access to court docket sheets and filed documents, contact the PACER Service Center at **www.pacer.pcs.uscourts.gov** or by phone at 1-800-676-6856 for a log-in and password.